a selectable marker
is selected from the group consisting of: a neomycin resistance gene; an acyclovir
resistance gene and a gancyclovir resistance gene.
13. The method according to any one of claims 1, 2, 6 or 7, further comprising
producing progeny of the transgenic mouse by breeding.
14. A method for producing a transgenic mouse wherein the germ cells comprise at
least one inactivated endogenous immunoglobulin light chain locus in which the
C.kappa. gene is deleted to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged locus and the expression of an endogenous
immunoglobulin light chain from the inactivated locus, said method comprising the
steps of:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of said locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker; and
(b) producing from the embryonic stem cell a transgenic mouse whose germ cells
comprise at least one immunoglobulin light chain locus in which the C.kappa. gene
is deleted.
15. A method for producing a transgenic mouse and its progeny, wherein the somatic
and germ cells comprise at least one inactivated endogenous immunoglobulin light
chain locus in which the C.kappa. gene is deleted to prevent rearrangement of the
locus and to prevent formation of a transcript of a rearranged locus and the
expression of an endogenous immunoglobulin light chain from the inactivated locus,
said method comprising the steps of:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a

selectable marker;
(b) producing from the embryonic stem cell a transgenic mouse whose germ cells
comprise at least one immunoglobulin light chain locus in which the C.kappa. gene
is deleted, and
(c) breeding the transgenic mouse as needed to produce a transgenic mouse and its
progeny whose somatic and germ cells comprise at least one inactivated endogenous
immunoglobulin light chain locus in which the C.kappa. gene is deleted.
16. The method according to claim 14 or 15, wherein the gene encoding a selectable
marker is selected from the group consisting of: a neomycin resistance gene; an
acyclovir resistance gene and a gancyclovir resistance gene.
17. A mouse embryonic stem cell with at least one inactivated endogenous
immunoglobulin light chain locus in which the C.kappa. gene is deleted to prevent
rearrangement of the locus and to prevent formation of a transcript of a rearranged
immunoglobulin light chain locus, said inactivated endogenous locus comprising a
gene encoding a selectable marker.
18. The mouse embryonic stem cell according to claim 17, wherein said gene encoding
a selectable marker is selected from the group consisting of: a neomycin resistance
gene; an acyclovir resistance gene and a gancyclovir resistance gene.
19. A transgenic mouse wherein the germ cells comprise at least one inactivated
endogenous immunoglobulin light chain locus in which the C.kappa. gene is deleted
to prevent rearrangement and to prevent formation of a transcript of a rearranged
locus and the expression of an endogenous immunoglobulin light chain from the
inactivated locus.
20. A transgenic mouse, wherein the somatic and germ cells comprise at least one
inactivated endogenous immunoglobulin light chain locus in which the C.kappa. gene
is deleted to prevent rearrangement and to prevent formation of a transcript of a
rearranged locus and the expression of an endogenous immunoglobulin light chain from
the inactivated locus.
21. A transgenic mouse, wherein the somatic and germ cells

comprise inactivated
endogenous immunoglobulin loci in which the C.kappa. gene is deleted to prevent
rearrangement and to prevent formation of a transcript of a rearranged locus,
wherein the transgenic mouse and progeny lack expression of endogenous
immunoglobulin light chains.

US-PAT-NO: 6114598
DOCUMENT-IDENTIFIER: US 6114598 A
TITLE: Generation of xenogeneic antibodies
DATE-ISSUED: September 5, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kucherlapati; Raju	Darien	CT	N/A	N/A
Jakobovits; Aya	Menlo Park	CA	N/A	N/A
Kalpholz; Sue	Stanford	CA	N/A	N/A
Brenner; Daniel G.	Redwood City	CA	N/A	N/A
Capon; Daniel J.	Hillsborough	CA	N/A	N/A

US-CL-CURRENT: 800/18,435/325 ,435/354 ,800/22 ,800/25 ,800/3 ,800/4

CLAIMS:

What is claimed is:

1. A mouse embryonic stem cell with at least one inactivated endogenous immunoglobulin heavy chain locus in which all of the J segment genes are deleted to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, said inactivated endogenous locus comprising a gene encoding a selectable marker.

2. The mouse embryonic stem cell according to claim 1, wherein said gene encoding a selectable marker is selected from the group consisting of: a neomycin resistance gene; an acyclovir resistance gene and a gancyclovir resistance gene.

3. A transgenic mouse wherein the germ cells comprise at least one inactivated endogenous immunoglobulin heavy chain locus in which all of the J segment genes are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin heavy chain from the inactivated locus.

4. A transgenic mouse or the progeny thereof, wherein the somatic and germ cells

comprise at least one inactivated endogenous immunoglobulin heavy chain locus in
which all of the J segment genes are deleted to prevent rearrangement and to prevent
formation of a transcript of a rearranged locus and the expression of an endogenous
immunoglobulin heavy chain from the inactivated locus.
5. A transgenic mouse or the progeny thereof, wherein the somatic and germ cells
comprise inactivated endogenous immunoglobulin loci in which all of the J segment
genes are deleted to prevent rearrangement and to prevent formation of a transcript
of a rearranged locus, wherein the transgenic mouse and progeny lack expression of
endogenous immunoglobulin heavy chains.

US-PAT-NO: 6150584
DOCUMENT-IDENTIFIER: US 6150584 A
TITLE: Human antibodies derived from immunized xenomice
DATE-ISSUED: November 21, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kucherlapati; Raju	Darien	CT	N/A	N/A
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Klapholz; Sue	Stanford	CA	N/A	N/A

US-CL-CURRENT: 800/18,424/93.21 ,800/25 ,800/6

CLAIMS:

What is claimed is:
1. A transgenic mouse wherein all of the somatic and germ cells comprise a DNA fragment of human chromosome 14 from the five most proximal V.sub.H gene segments, continuing through the D segment genes, the J segment genes and the constant region genes through C.delta. of the human immunoglobulin heavy chain locus, wherein said fragment does not contain a C.gamma. gene, and wherein said fragment is operably linked to a human C.gamma.2 region gene;
said transgenic mouse producing fully human IgG2 heavy chains specific for a desired antigen when immunized with said desired antigen.
2. The transgenic mouse according to claim 1, wherein all of the somatic and germ cells of said transgenic mouse further comprise a fragment of human chromosome 2 comprising V.sub..kappa., J.sub..kappa. and C.sub..kappa. gene segments of an immunoglobulin kappa light chain locus, said transgenic mouse producing fully human IgG2 antibodies specific for a desired antigen when immunized with said desired antigen.
3. The transgenic mouse according to claim 1, wherein all of the somatic and germ

cells comprise the human DNA contained in the yH1C YAC having ATCC accession no.
74367.
4. The transgenic mouse according to claim 2, wherein all of the somatic and germ
cells comprise the human DNA contained in the yH1C YAC having ATCC accession no.
74367.
5. The transgenic mouse according to claim 3, wherein said fragment of human
chromosome 2 extends from the three most proximal V.sub..kappa. gene segments,
continuing through the J.sub..kappa. and C.sub..kappa. gene segments, through the
human kappa deleting element.
6. The transgenic mouse according to claim 4, wherein said fragment of human
chromosome 2 extends from the three most proximal V.sub..kappa. gene segments,
continuing through the J.sub..kappa. and C.sub..kappa. gene segments, through the
human kappa deleting element.
7. The transgenic mouse and progeny according to any one of claims 1-6, wherein all
of the somatic and germ cells further comprise:
a) inactivated endogenous immunoglobulin heavy chain loci in which all of the J
segment genes are deleted to prevent rearrangement and to prevent formation of a
transcript of a rearranged locus and the expression of an endogenous immunoglobulin
heavy chain; and
b) inactivated endogenous immunoglobulin light chain loci in which the C.sub..kappa.
gene is deleted to prevent expression of an endogenous immunoglobulin light chain;
wherein said transgenic mouse and progeny lack expression of endogenous
immunoglobulin heavy chains.
8. A method for producing a fully human IgG antibody specific for a desired
antigen, comprising:
(a) immunizing a transgenic mouse according to any one of claims 1-7 with said
desired antigen; and
(b) recovering the antibody.
9. The method according to claim 8, wherein the desired antigen is selected from
the group consisting of: leukocyte markers; histocompatibility antigens;
integrins; adhesion molecules; interleukins; interleukin

receptors; chemokines;
growth factors; growth factor receptors; interferon receptors;
immunoglobulins
and their receptors; tumor antigens; allergens; viral
proteins; toxins; blood
factors; enzymes; ganglioside GD3, ganglioside GM2; LMP1,
LMP2; eosinophil major
basic protein, eosinophil cationic protein; pANCA; Amadori
protein; Type IV
collagen; glycated lipids; .gamma.-interferon; A7;
P-glycoprotein; Fas (AFO-1)
and oxidized-LDL.

10. The method according to claim 8, wherein the desired antigen is human IL-8.

11. The method according to claim 8, wherein the desired antigen is PTHrp.

12. The yH1C YAC having ATCC accession number 74367.

deletion being effected by a targeting vector comprising a gene encoding a
selectable marker; and
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain an immunoglobulin light chain locus in which the C.kappa. gene is
deleted,
wherein the transgenic mouse lacks expression of an endogenous immunoglobulin light
chain.
3. A method for producing a transgenic mouse and its progeny lacking expression of
endogenous immunoglobulin light chains, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker;
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain the gene encoding the selectable marker, and
(c) breeding the transgenic mouse as needed to produce a transgenic mouse and its
progeny lacking expression of endogenous immunoglobulin light chains.
4. A method for producing a transgenic mouse and its progeny lacking expression of
endogenous immunoglobulin light chains, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker;
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain an immunoglobulin light chain locus in which the C.kappa. gene is
deleted, and (c) breeding the transgenic mouse as needed to produce a transgenic
mouse and its progeny lacking expression of endogenous immunoglobulin light chains.
5. The method according to any one of claims 1-4, wherein the

gene encoding a
selectable marker is selected from the group consisting of: a neomycin resistance
gene; an acyclovir resistance gene and a gancyclovir resistance gene.
6. A method for preventing the expression of an endogenous immunoglobulin light
chain in a transgenic mouse, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker; and
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain the gene encoding the selectable marker,
wherein the transgenic mouse lacks expression of an endogenous immunoglobulin light
chain.
7. A method for preventing the expression of an endogenous immunoglobulin light
chain in a transgenic mouse, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker; and
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain an endogenous immunoglobulin light chain locus in which the C.kappa.
gene is deleted,
wherein the transgenic mouse lacks expression of an endogenous immunoglobulin light
chain.
8. A method for preventing the expression of endogenous immunoglobulin light chains
in a transgenic mouse and its progeny, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light

chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker;
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain the gene encoding the selectable marker, and
(c) breeding the transgenic mouse as needed to produce a transgenic mouse and its
progeny lacking expression of endogenous immunoglobulin light chains.
9. A method for preventing the expression of endogenous immunoglobulin light chains
in a transgenic mouse and its progeny, comprising:
(a) deleting the C.kappa. gene from at least one endogenous light chain locus in a
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent
formation of a transcript of a rearranged immunoglobulin light chain locus, the
deletion being effected by a targeting vector comprising a gene encoding a
selectable marker;
(b) producing from the embryonic stem cell a transgenic mouse whose somatic and germ
cells contain an immunoglobulin light chain locus in which the C.kappa. gene is
deleted, and
(c) breeding the transgenic mouse as needed to produce a transgenic mouse and its
progeny lacking expression of endogenous immunoglobulin light chains.
10. The method according to any one of claims 6-9, wherein the gene encoding a
selectable marker is selected from the group consisting of: a neomycin resistance
gene; an acyclovir resistance gene and a gancyclovir resistance gene.
11. A method for producing a mouse embryonic stem cell with at least one
inactivated endogenous immunoglobulin light chain locus, comprising deleting the
C.kappa. gene from at least one endogenous immunoglobulin light chain locus in the
mouse embryonic stem cell to prevent rearrangement of the locus and to prevent the
formation of a transcript of a rearranged immunoglobulin light chain, the deletion
being effected by a targeting vector comprising a gene encoding a selectable marker.
12. The method according to claim 11, wherein the gene encoding